

March 8, 2017

Submission Request
National Comprehensive Cancer Network® (NCCN)

RE: Clinical Evidence in Support of ZYKADIA® (ceritinib) for First-line Use in Anaplastic Lymphoma Kinase Positive (ALK+) Non-small Cell Lung Cancer (NSCLC)

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Date of request: March 8, 2017
NCCN Guidelines Panel: NSCLC

To Whom It May Concern:

As the NCCN NSCLC Panel reviews the Clinical Practice Guidelines in Oncology® (NCCN Guidelines) for Non-small Cell Lung Cancer version 4.2017 and the associated Drugs and Biologics Compendium™, we have enclosed data relating to treatment with ceritinib for your consideration:

- Data to support the first-line use of ceritinib in patients with ALK+ metastatic NSCLC

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Ceritinib for first-line use in ALK+ metastatic NSCLC

This request is for the Panel to consider including ceritinib as a treatment option in the first-line setting for ALK+ metastatic NSCLC.

In a randomized, open-label, phase 3 study (N=376) of ceritinib vs platinum-based chemotherapy, the median PFS was 16.6 months with ceritinib compared to 8.1 months with chemotherapy (HR 0.55 [95% CI 0.42–0.73]; $P < 0.00001$). The most common AEs were diarrhea (85%), nausea (69%), vomiting (66%), and increased ALT (60%) with ceritinib and nausea (55%), vomiting (36%), and anemia (35%) with chemotherapy.¹

Specific changes recommended for the Guidelines & Compendium

Please consider modifying section NSCL-20, and relevant discussion and reference, to include ceritinib as a treatment option for first-line therapy for ALK+ metastatic NSCLC.

FDA status

Ceritinib is not FDA-approved in the first-line setting for ALK+ metastatic NSCLC. Ceritinib is a kinase inhibitor indicated for the treatment of patients with ALK+ metastatic NSCLC who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or

disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Rationale for recommended change

The results of this study demonstrate the safety and efficacy of ceritinib in the first-line setting for patients with ALK+ metastatic NSCLC.¹

Literature support

1. Soria J-C, Tan D SW, Chiari R, et al. First-line ceritinib vs. platinum-based chemotherapy in advanced ALK-rearranged NSCLC (ASCEND-4): a randomised, open-label, phase 3 study. *Lancet*. 2017 Jan 23 (Epub ahead of print)

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We appreciate the opportunity to provide this additional information for consideration by the NCCN NSCLC Panel. If you have any questions or require additional information, please do not hesitate to contact me at 862-778-5494 or via e-mail at neilda.baron@novartis.com. Thank you for your time and consideration.

Sincerely,

Neilda Baron, MD
Executive Director and Head, US Oncology Medical Information
Novartis Pharmaceuticals Corporation

Enclosures: Copy of referenced publication and Zykadia Prescribing Information
Disclosures included within publication